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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,818	07/19/2006	Marie Dutreix	BJS-3665-177	2272

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
08/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,818	DUTREIX ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-30 and 32-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-30 and 32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group 2 in the reply filed on May 19, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

All claims to non-elected inventions have been canceled. Claims 17-30 and 32-38 are directed to the elected invention and examined.

Claim Objections

Claims 21, 25-27 and 29 are objected to because of the following informalities:

-claim 21 recites that the molecule inhibits in vitro radiation-enhanced illegitimate exogenous DNA integration. The specification describes at page 29 that the phrase " radiation-enhanced illegitimate exogenous DNA integration" is also known as radiation enhanced integration, but the use of the words in vitro in this claim is ambiguous, it is unclear whether this claim is meant to state that inhibition occurs only in cells in vitro or if the inhibition only occurs when the radiation is applied in vitro.

-in line 2 of claim 25 it appears that a zero is used rather than a letter "O" in the phrase 2'-O,4'-C.

-claims 26 and 27 each refer to "the 3' end strand". While it is recognized that the individual strands of a double stranded nucleic acid have a 3' end, there is no art

recognized definition for a portion of a nucleic acid being a 3' end strand. This phrase has been interpreted as referring to the 3' end of an individual strand comprising the claimed double strand portion.

-in claim 29, limitation b) is grammatically awkward, defining a unit as a blocking element as it is not amenable by DNA polymerases. Based on the specification at page 15, second paragraph, it appears that these elements are moieties not recognized by DNA polymerases, it is suggested that this limitation be amended to clarify this as the purpose of a blocking element.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 28 recites the limitation that the nucleic acid molecule used in the claimed method comprises an embedded element that hampers a damage signaling process. While pages 14-15 of the specification disclose that the nucleic acid molecules may

have elements such a non-nucleic acid portion that prevents DNA replication or a modified nucleotide that is not recognized by cellular polymerases, the specification is silent with regard to description of what elements can hamper a damage signaling process. Claim 29 depends from claim 28 and recites that the molecule can comprise one of three elements; polyethylene glycol, a blocking element not recognized by DNA polymerases, and a native oligonucleotide, however based on the disclosure of the specification it is not clear if any of these specific components would be an element that hampers a damage signaling process. Those of skill in the art are aware from the teachings of the prior art of the components of the DNA damage signaling pathways and how these proteins interact to repair DNA damage. However, the prior art does not disclose what elements can be incorporated into a nucleic acid that will provide the function of hampering such damage signaling processes. In view of the complicated nature of DNA damage signaling processes in terms of the number of component proteins and the degree of interactions between these proteins to signal DNA damage and the lack of description of elements that can be incorporated into a nucleic acid and provide the function of hampering any of these proteins and/or interactions, claims 28 and 29 do not satisfy the written description requirement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-27, 30 and 32-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omori (cited on IDS) in view of Marthinet et al. (Gene Therapy 2000, vol 7, pages 1224-1233) and Klem (US 2003/0176376).

The claims are directed to methods of enhancing tumor sensitivity and treating cancer by administering a double stranded nucleic acid of at least 16 bp that is a substrate for a Ku protein involved in the NHEJ pathway in combination with a DNA damaging agent. The nucleic acid can be prior to or along with the additional therapy, can be used to treat several types of cancer and is administered by routes that include direct intratumoral injection. Specific claims recite that the nucleic acid is 16-200 bp, is a linear or a hairpin nucleic acid, the free end is blunt or overhanging, the nucleic acid comprises modified nucleotides such as modified backbones, sugars or nucleobases, and the nucleic acid is synthesized chemically or biologically. The claims further recite

that the nucleic acid inhibits in vitro radiation-enhanced illegitimate exogenous DNA integration and is capable of being taken up into the cell nucleus.

Omori et al. teach that Ku70 protein is involved in DNA double-strand break repair and Ku70-deficient cells have increased radiosensitivity to ionizing radiation. Omori et al. use an antisense oligonucleotide targeted to Ku70 to suppress Ku70 protein expression in human squamous cell lung carcinoma cell line. The antisense treated cells were more radio- and chemosensitive than the parental cells. Omori et al. note that because clinical cancer radiotherapy is usually performed in multiple fractions, even a small increase in radiosensitivity at a low dose would yield significant differences in biological effect and suggest that inhibition of Ku70 could be applied therapeutically. Omori et al. do teach the use of double stranded decoy molecules to suppress Ku70.

Marthinet et al. teach on page 1225, first column that antisense oligonucleotides are a known strategy to modify expression of genes responsible for malignancy and resistance to therapy. Marthinet et al. further teach that double-stranded oligodeoxynucleotides designed to reproduce regulatory *cis*-elements have been used in a new class of anti-gene strategy and have been successfully applied to several diseases. Marthinet et al. teach the use of both antisense oligonucleotides and double stranded decoy oligonucleotides to block expression of the MDR phenotype in cancer cells. The teachings of Marthinet et al. demonstrate that both antisense and decoy based therapy is effective and provides evidence that the two approaches are equivalent.

At the time the invention was made those of ordinary skill in the art were well aware of the design principles of decoys such as the use of modified nucleotides and that cancer treatment routinely involves combination of nucleic acid therapies with other chemotherapeutic agents. Klem exemplifies these concepts; teaching that cancer treatment with decoy oligomers can be performed with other therapies, defined at paragraph 29 as including radiation therapy. Klem further teaches at paragraphs 61-64 that decoys can comprise modified nucleotides, including modified backbone moieties such as phosphorothioate and methylphosphonate, and are generally at least 16 bases in length. Klem further teaches that these agents can be administered by a variety of routes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a decoy molecule targeted to a Ku protein to enhance tumor sensitivity or treat cancer by administration in combination with another cancer therapy. Omori et al. provide a reason to target proteins involved in double strand break repair by teaching that inhibition of Ku70 increases radiation sensitivity of tumor cells and suggest this is a viable therapeutic target. Based on the teachings of Marthinet et al. and Klem, one of ordinary skill in the art would recognize that decoy oligomers are an equivalent agent to the antisense oligonucleotides used by Omori et al. and that the use of one over the other is simple substitution of one known element for another. Based on the teachings of Klem of how to make decoys, administer them and combine them with other cancer therapies, one of ordinary skill in the art would be motivated and have a reasonable expectation of success in making decoys with these characteristics and

using them therapeutically. Because these decoys meet the structural limitations of the claims they are assumed in the absence of evidence to the contrary to provide the functions recited in claims 21 and 22.

Thus, the invention of claims 17-27, 30 and 32-38 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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